Practitioner's Docket No. 701826-073080 ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Laurent Bazinet et al.		
Application No.:	10/591,238	Art Unit:	1724
Filing or 371 (c) Date:	05-14-2007	Examiner:	RAPHAEL, COLLEEN M
Confirmation No.:	9269		
For:	Process And System For Separation Of Organic Charged Compounds		

2nd DECLARATION BY Dr. LAURENT BAZINET

I, Laurent Bazinet, Ph.D., pursuant to 37 C.F.R. 1.132 hereby declare as follows:

1. I am a citizen of Canada and I am a professor at the Department of Food Science and Nutrition, Faculty of Food Science of Université Laval, Québec city, Canada.
2. A copy of my *curriculum vitae* has been submitted earlier with my first Declaration.
3. I am a co-inventor of the above-identified application.
4. I have reviewed the above-identified patent application and the Office Action dated October 26, 2011 and the references cited by the examiner.
5. In view of the Office Action, I understand that the examiner concluded that a skilled scientist would have come up with the presently claimed invention by combining the following references: US Patent No. 4,322,275 ("Jain"); U.S. Patent No. 3,046,211 ("Tye"); U.S. Patent No. 5,437,774 ("Laustsen"); U.S. Patent Application Publication No. 2002-0102339 ("Akashe"); U.S. Patent No. 6,312,578 ("Canivenc"); U.S. Patent No. 6,649,037 ("Liang"); U.S. Patent No. 4,123,342 ("Ahlgren"); and U.S. Patent Application Publication No. 2003-0213748 ("Jangbarwala").
6. I disagree with the examiner's conclusion for the reasons explained in detail as follows.
7. I have been asked to describe why it is my opinion that a scientist working on the area of membrane separation would not have combined the references cited by the examiner.
8. In my first Declaration, I addressed Jain and Tye. The following supplements my previous statements and in addition to Jain and Tye, also specifically addresses Laustsen and Ahlgren.
9. Membrane separation processes are based upon selective permeability of one or more of the liquid constituents through a **membrane** according to a **driving force** (Bazinet and Firdaous, Recent Patents on Biotechnology 2009, 3, 61-72, p. 61, second col., submitted herewith as **Exhibit A**).

10. The **membranes** can be (1) porous, such as filtration, e.g., ultrafiltration membranes, and (2) non-porous, such as electrodialysis membranes. (Bazinet et al., 2007, Separation Science and Technology 42:11, 2501-2518, submitted herewith as **Exhibit B**).
11. The **driving forces** that allow separation of molecules through the membranes include (1) pressure difference which is used to drive molecules through a porous or filtration membranes, such as in ultrafiltration membrane, and (2) electrical potential which is used in connection of non-porous ion-exchange membranes to separate molecules according to their charge (Bazinet and Firdaous, Recent Patents on Biotechnology 2009, 3, 61-72, p. 61, second col.).
12. Pressure has been used in driving molecules through porous or filtration membranes because porous or filtration membranes are relatively thick and conduct electricity very poorly (Bazinet et al., 2007, Separation Science and Technology 42:11, 2501-2518). Thus porous membrane would not be expected to pass molecules effectively through with electrical force alone.
13. Moreover, if one were to consider using only electrical current, one would not expect such a system to work. This is because of the **known low conductivity of the UF membrane** would be expected to result in high energy consumption in such system (Bazinet et al., 2007, Separation Science and Technology 42:11, 2501-2518). Increasing the amount of electrical current in such high energy consumption system would eventually be expected to lead to water dissociation (Id.). Water dissociation in turn would be expected to result in a drastic pH increase at the CEM-diluate and AEM-concentrate interfaces and a proportional decrease at the AEM-diluate and CEM concentrate interfaces (Id.). Such pH changes would be problematic in, e.g., protein purification as proteins are susceptible for denaturation as the pH changes. Moreover, it has also been shown that a higher electric field does not allow separation between different small molecules (see, e.g., Aider et al. figures 1-3 on page 66, attached herewith as **Exhibit C**).
14. Of all the references cited by the examiner, only Ahlgren and Laustsen appear to describe a system, which combines a use of ED and a filtration membrane in some way. Both Ahlgren and Laustsen specifically use pressure to drive molecules through the filtration membrane. None of the remaining cited art describes a system with filtration membranes, such as UF membranes as currently claimed.
15. None of the cited references also provides description to teach or suggest that electrical forces alone would be suitable for the use with a filtration membrane, particularly with a UF membrane as currently claimed. Further, none of the cited references provide any guidance why one would expect electrical current to work in view of the known problems associated with the low electrical conductivity of the filtration membrane, such as UF membrane.

16. As evidenced by, e.g., Ahlgren, cited by the examiner, separation using **UF membranes** has traditionally used **pressure as driving force**. Ahlgren itself describes a combination of ED and a UF apparatus which uses significant amount of pressure. Ahlgren also states that "… cells 33c are suitably supported so that they can withstand the **pressures commonly employed in filtration systems**, e.g., on the order of 10-100 pounds psi or more" (col. 2, lines 20-24, emphasis added).
17. In the Office Action, the examiner stated that

> …it would have been obvious to one with ordinary skill, in the art at the time of filing to modify the method of Jain by operating the cell with **no pressure differential** between the cell compartments as taught by Tye, **because this would optimize the flow rate through the membranes** from the concentrating liquid to the desalting liquid… (par. bridging pages 4 and 5 of the Office Action).

18. On page 11, the examiner also stated that

> Even if Jain is interpreted as being silent on whether the neutral membrane is a filtration membrane, it would be obvious … to apply the teachings of Laustsen to the process of Jain, as both Jain and Laustsen are drawn to methods of separating proteins by electrodialysis.

19. The examiner interpreted that the neutral membrane in Jain is a filtration membrane. However, this statement ignores the scientific facts in that this is not so. The combination of Jain with Tye only teaches a system with ED membranes, not a combination of ED with a filtration, particularly, UF membrane. Neither Jain nor Tye use a system which combines ED and a filtration membrane to separate molecules.
20. Also, contrary to the examiner's statement, in col. 3 lines 33-36 **Tye does not describe a filtering system without pressure differences**. Tye specifically talks about **uniform pressure differences** explicitly **requiring pressure difference to exist** between the ED membrane bound compartments. Lines 33-46 of Tye (partially cited by the examiner) read as follows:

> It is clear, therefore, that there will be an optimum rate of flow through the membranes from the concentrating liquid to the desalting liquid with any given liquids in any given cell. It is obviously desirable to try to attain this flow rate in all parts of the cell, and this means that **the pressure difference** across the membranes **must be fairly uniform** throughout the cell… it is possible by adjustment of flow rates and valves, to arrange that the **same pressure difference** exists between the streams 13 and 11 as between the streams 14 and 12, 17 and 15, and 18 and 16, so that the pressure difference across the membranes 0-4 and 6-10 is the same. However, the pressure difference across the membrane 5 is different… (emphasis added)

21. This citation does not teach a system without pressure difference, quite the contrary, it **teaches using a uniform or same pressure difference**.
22. Even if one were to interpret Tye as describing a system which worked without "pressure differential", in view of the fact that Tye only describes systems which have ED membranes, a skilled artisan knowing that filtration membranes, such as UF membranes have poor conductivity would not have considered using a system without pressure, e.g., a system with electrical current alone in a cell that includes a combination of ED and UF membranes.
23. Laustsen, which appears to describe combined use of a filtration membrane and ED, also specifically **used pressure difference** to drive the molecules through the filtration membrane.
24. Neither Laustsen, nor Ahlgren, which are the only references that have a UF membrane in the system, describe any conditions that would allow pushing molecules through a UF membrane without pressure differential.
25. In view of the knowledge in the field regarding poor electrical conductivity of filtration membranes, even if one would have considered using no pressure in an ED/UF system, one would not have expected the UF membrane to pass through useful amounts of molecules if no pressure was applied to assist driving the molecules through it. Moreover, one would have expected a high likelihood of denaturation of any proteins one would have tried to isolate with such a method either due to pH or temperature changes as described above.
26. We discovered a way to overcome these problems by conditioning the UF membrane. None of the prior art references teaches a cell that uses ED and a conditioned UF membrane.
27. Thus, we discovered a particular optimization step that allows the combination of electrodialysis with ultrafiltration to operate without pressure using conditioning of the UF membrane. We discovered that conditioning allowed the molecules to pass through the UF membrane with electrical current only, without running into the requirement of high energy consumption and problems associated with it.

28. I hereby declare that all statements made of our own knowledge are true and that all statements made on information and belief are believed to be true, and that willful false statements and the like are punishable by fine or imprisonment, or both under 18 U.S.C. §1001, and may jeopardize the validity of the application or any patent issuing thereon.

Signature: _____ Date: February 23th 2012

Laurent Bazinet